New Drug Approvals
2017 & 2018

In the next 60 minutes…
• Discuss the statistics of drug approvals in the United States in 2017
• Review the mechanisms, side effects, and key counseling points for many of the new drugs
• List notable changes in drug formulations and indications
• Consider improved competition for generic drug approval
• Outline the process by which drug safety data is reported and distributed
• Offer resources for staying up-to-date on new drug approvals and labeling changes

You will learn…
• 2017 was a record-setting year for drug approvals
• Cancer and infectious disease indications dominated approvals
• Biosimilar approvals soared in 2017
• The rate of first-in-class approvals is declining
• FDA has established new priorities to speed drug approval and improve sharing of safety information
2017 – Back on Track

• The FDA approved 46 novel drug applications
  – More than double the number of new approvals in 2016
  – Represents a 21-year high
• 5 new biosimilars approved
• Several cell and gene therapies approved

Highs and Lows of Innovation

• Most products approved under accelerated pathways
  – “Breakthrough therapy” designations nearly doubled from 2015
• New paradigms for treating serious diseases
  – 37% of drugs considered first-in-class

New Molecular Entities
Emflaza (deflazacort)

- Treats Duchenne muscular dystrophy in patients 5 years and older
- Anti-inflammatory and immunosuppressive effects
- Supplied as oral tablets and an oral suspension
  - Recommended dose: 0.9 mg/kg once daily
- Side effects
  - Increased weight
  - Increased appetite
  - Hirsutism
  - Upper respiratory tract infection

Xermelo (telotristat ethyl)

- Treats carcinoid syndrome diarrhea in combination with somatostatin analog in adults
- Tryptophan hydroxylase inhibitor
- Supplied as oral tablet
  - Recommended dose: 250 mg 3 times daily
- Side effects
  - Severe constipation
  - Gastrointestinal upset
  - Depression
  - Peripheral edema

Dupixent (dupilumab)

- Treats moderate-to-severe eczema in adults
- Interleukin-4 receptor alpha antagonist
- Supplied as solution for SC administration
  - Recommended dose: 600 mg once, then 300 mg every other week
- Side effects
  - Injection site reactions
  - Ophthalmologic issues
  - Oral herpes and other herpes simplex virus infections
Ocrevus (ocrelizumab)

- Treats relapsing and primary progressive forms of multiple sclerosis
- CD20-directed cytolytic antibody
- Supplied as solution for IV administration
  - Recommended dose: 2 infusions (300 mg each) separated by 2 weeks, then 600 mg every 6 months
- Side effects
  - Upper respiratory tract infections
  - Infusion reactions

Austedo (deutetrabenazine)

- Treats chorea associated with Huntington’s disease and tardive dyskinesia
- VMAT2 inhibitor
- Supplied as oral tablets
  - Recommended dose
    - Chorea: initially 6 mg once daily
    - Tardive dyskinesia: initially 12 mg once daily
    - Increase to maximum of 48 mg daily
- Side effects
  - Somnolence and fatigue
- Black box warning: depression and suicidality

Brineura (cerliponase alfa)

- Treats a specific type of Batten disease (late infantile neuronal ceroid lipofuscinosis)
- Hydrolytic lysosomal N-terminal tripeptidyl peptidase
- Supplied as injection for intraventricular administration
  - Recommended dose: 300 mg every other week
- Side effects
  - ECG abnormalities
  - Changes in levels of CSF protein
  - Headache
Rydapt (midostaurin)
- Treats acute myeloid leukemia and mastocytosis
- Multikinase inhibitor
- Supplied as capsule for oral administration
  - Recommended dose
    - AML: 50 mg orally twice daily on days 8 to 21 of cytarabine/daunorubicin
    - Mastocytosis: 100 mg twice daily
- Side effects
  - Nausea, vomiting, diarrhea
  - Headache
  - Musculoskeletal pain
  - Upper respiratory tract infection

Radicava (edaravone)
- Treats amyotrophic lateral sclerosis (ALS or Lou Gehrig’s Disease)
- Free radical scavenger
- Supplied as infusion for IV administration
  - Recommended dose: 60 mg over 60 minutes
  - Alternate daily administration with drug-free periods
- Side effects
  - Contusion
  - Gait disturbance
  - Headache

IDHIFA (enasidenib)
- Treats relapsed or refractory acute myeloid leukemia
- Small molecule inhibitor of the IDH2 enzyme
- Supplied as oral tablets
  - Recommended dose: 100 mg once daily
- Side effects
  - Nausea, vomiting, diarrhea
  - Decreased appetite
- Black box warning: fatal differentiation syndrome possible
### Besponsa (inotuzumab ozogamicin)
- Treats relapsed or refractory acute lymphoblastic leukemia
- CD22-directed antibody-drug conjugate
- Supplied as solution for IV injection
- Side effects
  - Hematologic abnormalities
  - Infection
  - Nausea and abdominal pain
- Black box warning: severe hepatotoxicity has occurred

### Kymriah (tisagenlecleucel)
- Treats refractory acute lymphoblastic leukemia
- CD19-directed genetically modified autologous T-cell immunotherapy
- Supplied as suspension for IV infusion
- Side effects
  - Encephalopathy
  - Kidney injury
  - Delirium
- Black box warning: cytokine release syndrome, neurological toxicities

### Yescarta (axicabtagene ciloleucel)
- Treats relapsed or refractory large B-cell lymphomas
- CD19-directed genetically modified autologous T-cell immunotherapy
- Supplied as suspension for IV infusion
- Side effects
  - Encephalopathy
  - Infection
  - Kidney injury
  - Gastrointestinal upset and decreased appetite
- Black box warning: cytokine release syndrome, neurological toxicities
**Shingrix (zoster vaccine recombinant, adjuvanted)**

- Vaccine against virus that causes shingles
- Indicated for patients aged 50 years and older
- Supplied as lyophilized antigen that must be reconstituted prior to IM administration
  - Administered as 2 doses 2 to 6 months apart
- Side effects
  - Pain at injection site
  - Myalgia

**Prevymis (letermovir)**

- Prevents infection after bone marrow transplant
- Cytomegalovirus DNA terminase complex inhibitor
- Supplied as an oral tablet and a solution for IV infusion
  - Recommended dose: 480 mg once daily through 100 days post-transplant
- Side effects
  - Nausea, vomiting, diarrhea, abdominal pain
  - Peripheral edema

**Mepsevii (vestronidase alfa-vjbk)**

- Treats adults and children with Sly syndrome (mucopolysaccharidosis VII)
- Recombinant human lysosomal beta glucuronidase
- Supplied as a solution for IV infusion
  - Recommended dose: 4 mg/kg every 2 weeks
- Side effects
  - Infusion site reactions and extravasation
- Black box warning: anaphylaxis has occurred as early as first dose
Hemlibra (emicizumab-kxwh)
- Treats adults and children with hemophilia A
- Bispecific factor IXa- and factor X-directed antibody
- Supplied as a solution for SC injection
  - Recommended dose: 3 mg/kg weekly for 4 weeks, then 1.5 mg/kg weekly
- Side effects
  - Injection site reactions
  - Headache
  - Joint pain
- Black box warning: thrombotic events

Rhopressa (netarsudil)
- Treats elevated intraocular pressure in patients with glaucoma or ocular hypertension
- Rho kinase inhibitor
- Supplied as a solution for ophthalmic administration
  - Recommended dose: 1 drop in the evening
- Side effects
  - Instillation site pain
  - Conjunctival and corneal abnormalities

Luxturna (voretigene neparvovec)
- Treats vision loss due to inherited retinal disease
- Gene therapy for mutations in RPE65 gene
- Supplied as an intraocular suspension for subretinal injection
- Side effects
  - Retinal tears
  - Cataract
  - Conjunctival and corneal abnormalities
Expanded Indications

- Bunavail (buprenorphine/naloxone)
  - Can now be used to initiate treatment with buprenorphine in opioid-dependent patients
  - Previously approved for maintenance treatment phase of opioid dependence treatment

Expanded Indications

- Victoza (liraglutide)
  - Reduces the risk of major adverse cardiovascular events in patients with T2D
  - Now the only T2D treatment with this indication
  - Initially approved for adjunct to diet and exercise to improve glucose control in adults with T2D

Expanded Indications

- Repatha (evolocumab)
  - Prevention of heart attacks, strokes, and coronary revascularizations
  - First PCSK9 inhibitor to receive this indication
  - Also approved as monotherapy or in combination with lipid-lowering drugs to reduce LDL cholesterol
New Combinations and Formulations

- AirDuo RespiClick (fluticasone propionate/salmeterol)
  - Twice-daily treatment of asthma in patients 12 years and older
  - Administered with RespiClick breath-activated, multi-dose dry powder inhaler
  - Launched at the same time as its generic
    - First and only generic fluticasone propionate/salmeterol inhaler

New Combinations and Formulations

- Noctiva (desmopressin acetate nasal spray)
  - Treats nocturia in adults
    - Only FDA-approved treatment
  - Should not be used by patients with symptomatic CHF, uncontrolled hypertension, and certain nasal conditions

New Combinations and Formulations

- Qtern (dapagliflozin/saxagliptin)
  - Combination of SGLT-2 inhibitor and DPP-4 inhibitor to treat T2D
    - Glyxambi (empagliflozin/linagliptin)
    - Steglujan (ertugliflozin/sitagliptin)
    - Not approved for T1D
New Combinations and Formulations

• Trelegy Ellipta (fluticasone furoate/umeclidinium/vilanterol)
  – Maintenance treatment of patients with COPD
  – First once-daily treatment with 3 active ingredients
  – Breo ellipta contains fluticasone furoate and vilanterol
  – Incruse ellipta contains umeclidinium

Biologic Drug Products

• Originators
• Biosimilars
• Interchangeables

Biosimilars in 2017

• Ogivri (trastuzumab-dkst)
• Mvasi (bevacizumab-awwb)
• Cyltezo (adalimumab-adbm)
• Renflexis (infliximab-adba)
• Ixifi (infliximab-qbtx)
Ogivri (trastuzumab-dkst)
- Biosimilar to Herceptin
- Approved December 1, 2017
- Launch date undisclosed under settlement agreement

Mvasi (bevacizumab-awwb)
- Biosimilar to Avastin
- Approved September 14, 2017
- No launch date announced
- Litigation pending

Cyltezo (adalimumab-adbm)
- Biosimilar to Humira
- Approved August 25, 2017
- No launch date announced
- Litigation pending
Renflexis (infliximab-adba)
- Biosimilar to Remicade
- Approved April 21, 2017
- Launched in U.S. in July 2017

Ixifi (infliximab-qbtx)
- Biosimilar to Remicade
- Approved December 13, 2017
- No current plans for U.S. launch

Looking Ahead
- Approvals expected for at least 7 new biosimilars
  - Pegfilgrastim
  - Filgrastim
  - Rituximab
  - Trastuzumab
  - Adalimumab
Looking Ahead
• Several biologics applications will receive action in 2018
  – Erenumab – prevention of migraines
  – Plasminogen – replacement therapy
  – Burosumab – treatment of X-linked hypophosphatemia
  – Denosumab – treatment of glucocorticoid-induced osteoporosis

Looking Ahead
• Many products focus on novel mechanisms
  – Halobetasol propionate and tazorotene – lotion for treating plaque psoriasis
  – Aripiprazole lauroxil nanocrystal dispersion – bridge initiation to extended-release injectable suspension for the treatment of schizophrenia
  – Fostamatinib disodium – treat immune thrombocytopenia

Looking Ahead
• Existing drugs seeking expanded indications and formulations
  – Buprenorphine sublingual spray – acute pain
  – Ferumoxytol – iron deficiency anemia
  – Ciprofloxacin otic suspension – acute otitis externa
  – Bupivacaine liposome injectable suspension – administration via nerve block for prolonged regional anesthesia
Looking Ahead
• Potential blockbusters on the horizon
  – Biologics
  – Gene therapy
  – Immunology
  – Neurology
  – Oncology
  – Pain

Looking Ahead
• FDA goals for 2018 include speeding up generic approvals and enhancing competition
  – Avoid delays in review process
  – Decrease number of review cycles

Labeling Changes
• FDA announced “safety labeling changes” (SLC) program
  – Moves available safety information from MedWatch to SLC databases
  – Enables information to be organized and distributed easily
• New rules have been proposed to speed up labeling changes
For more information, visit...

- Drug approval information
- FDA-approved drugs by year and class
- Biologics License Applications
  - https://biosimilarsrr.com/us-biosimilar-filings/
- Drug safety labeling changes

Thank You!

Speaker Contact Information:

Jennifer L Gibson, PharmD
Excalibur Scientific, LLC
Phone: (678) 689-4526
Email: JLGibson@ExcaliburScientific.com